Remarks

A Request for Continued Examination is made in this Reply to the Office Action dated October 24, 2006, (PTO Prosecution File Wrapper Paper No. 20061018, hereinafter "OA") and the Advisory Action of February 21, 2007, (PTO Prosecution File Wrapper Paper No. 20070209, hereinafter "AA").

Reconsideration of this Application is respectfully requested. Claims 3 and 47-49, 51-66 and 71-80 are pending in the application, with claims 3, 47-49, 71 and 76 being the independent claims. Claims 51-66 are withdrawn from consideration. Claims 3 and 47-49, 71 and 76 are pending and under consideration. Claims 50 and 67-70 are sought to be canceled without prejudice or disclaimer of the subject matter therein. New claims 71-80 are sought to be added. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Claims 47-49 have been amended to place them in better form for allowance or appeal. Claims 71-80 have been added to more clearly define the subject matter of the present invention. Support for these amendments may be found, *inter alia*, in the specification as-filed at paragraphs [0003], [0005], [0009], [0017], [0022-0025], [0028], [0032], [0033], [0036], [0037], [0042], [0049], [0060-0064], [0068], [0069], Examples 1-7 [0073-0087], Examples 8-11 [0090-0102] and Table 1. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Claim 49 has been amended to specifically encompass those sequences of the specification that fall within the limitation "at least 83 % identical to SEQ ID NO: 115." Support for this amendment can be found in the claims as originally filed.

Applicants submit that there is no serious burden on the Office to search the sequences recited in presently pending claim 49. A review of the sequence search report generated by the Examiner shows that the art in the area of scorpion toxins having similarity to SEQ ID NO: 115 is not crowded. The search report reveals that there are no sequences in the art that come within 80 % (based on the query match) and 88% (based on the best local similarity) of the sequence of SEQ ID NO:115. Thus, the search of SEQ ID NO: 115 previously conducted by the Examiner provides evidence that there is no serious burden on the Office to individually search each of the sequences claimed in presently-amended claim 49. The only sequences identified by the Examiner in his search that are related to SEQ ID NO: 115 are sequences disclosed by the inventors in the present application.

A proper restriction requires a showing that the inventions are independent (*See* MPEP §802.01, §806.04, §808.04), **and** there must be a serious burden on the Examiner to search the independent invention (*See* MPEP §803.02, §806.04(a), §806.04(i), §808.01(a) and §808.02). Here, the Examiner cannot establish that there is a serious burden to search the sequences in claim 49, because the search that was already conducted by the Examiner for SEQ ID NO:115 does not show that this area in the art is crowded. The search for SEQ ID NO: 115 did not reveal any similar sequences other than those disclosed by applicant in the present application. Thus, the inclusion of the additional sequences to claim 49 does not pose a serious burden on the Examiner.

Based on the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

Election/Restriction

Claims 51-66 have been withdrawn by the Examiner as allegedly being directed to a non-elected invention. (OA at page 2.) Applicants respectfully traverse the withdrawal of the claims from examination.

The Examiner has withdrawn claims 51-66 as allegedly being directed to a distinct invention from the compositions recited in claims 3 and 47-49. (OA, at page 2.) The Examiner asserts that "[s]ince applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation of prosecution on the merits," citing MPEP § 821.03. (*See Id.*) Applicants respectfully traverse the withdrawal of claims 51-66.

A. Claims 54, 58, 62 and 66

Applicants respectfully assert that claims 54, 58, 62 and 66 should be rejoined with the claims under consideration in the present application because they depend from either allowable claim 3 or claims 47-49, which are also believed by Applicants to be in condition for allowance. (*See* pages 12-19, *infra*). Presently-withdrawn claims 54, 58, 62 and 66 are directed to a method for producing a polypeptide using the nucleic acid sequences recited in claims 3 and 47-49 (*i.e.*, the nucleic acid sequence of SEQ ID NO: 115 and sequences having 95% or 99% identity with SEQ ID NO:115). The USPTO published a Notice in the March 26, 1996 Official Gazette setting forth the guidelines for the treatment of product and process claims in light of the Federal Circuit's decisions in *In re Ochiai*, 71 F.3d 1565 (Fed. Cir. 1995), and *In re Brouwer*, 77 F.3d 422 (Fed. Cir. 1996). *See* 1184 OG 86 (March 26, 1996). Specifically, the Notice states that in the case of an elected product claim, rejoinder will be permitted when a product claim is found

allowable and the withdrawn process claim depends from or otherwise includes all the limitations of an allowed product claim. *See Id.*

In the present case, the Examiner has restricted between the product recited in claims 3 and 47-49, and methods of using the product, as recited in claims 54, 58, 62 and 66. In the Office Action dated October 24, 2006, the Examiner stated that claim 3 is allowable because "the prior art does not describe an isolated nucleic acid comprising SEQ ID NO:115." (OA at page 4). Although the Examiner has rejected claims 47-49 under 35 U.S.C. §112, first paragraph, Applicants believe this rejection will be overcome, and that presently-pending claims 47-49 are in condition for allowance. (*See* pages 12-19, *infra*). Thus, in view of the guidelines set forth in the March 26, 1996 Official Gazette Notice, as well as the Federal Circuit's decisions in *In re Ochiai* and *In re Brouwer*, Applicants respectfully request reconsideration and rejoinder of withdrawn method claims 54, 58, 62 and 66 with presently-pending product claims 3 and 47-49. *See* 71 F.3d 1565 (Fed. Cir. 1995), *see also*, 77 F.3d 422 (Fed. Cir. 1996).

B. Claims 51-70

The Examiner has also withdrawn claims 51-70 from consideration, asserting that they are directed to distinct compositions "such as a genetically engineered host cell, comprising a recombinant vector comprising a distinct polynucleotide sequence." (OA at page 2.) Applicants respectfully traverse this restriction.

(i) Claims 51-53

Claims 51-53 should be rejoined and fully examined for patentability in accordance with 37 CFR §1.104 because they were presented for examination prior to final rejection or allowance, and require all the limitations of allowable claim 3. *See*

MPEP §821.04(a). Claims 51-53 depend directly or indirectly from claim 3, and are directed to compositions requiring the allowable product of claim 3 (SEQ ID NO: 115). In the Office Action of October 24, 2006, the Examiner essentially restricted claims 51-53 from the present application by withdrawing them as allegedly being directed to a non-elected invention. (OA at page 2). Applicants respectfully traverse this restriction.

Section 821.04(a) of the MPEP states that an amendment presenting additional claims that depend from, or otherwise require all the limitations of, an allowable claim ***will be entered as a matter of right*** if the amendment is presented prior to final rejection or allowance, whichever is earlier. *See* MPEP 821.04(a). In this case, the additional claims presented in the September 13, 2006 Amendment and Reply (including claims 51-53) were submitted before a final rejection was issued. Additionally, the Examiner has indicated that claim 3, directed to the nucleic acid sequence of SEQ ID NO:115, is allowable. (*See* OA, page 4). Claims 51-53 depend directly or indirectly from claim 3, and recite compositions requiring the allowable product of claim 3 (SEQ ID NO: 115). Claims 3 is a generic linking claim with regard to claims 51-53. *See* MPEP §809. When all claims directed to the elected invention are allowable, should any linking claim be allowable, the restriction requirement between the linked inventions must be withdrawn. *See* MPEP §809. Any claims directed to the nonelected invention(s), previously withdrawn from consideration, and which depend from or require all the limitations of the allowable linking claim must be rejoined and will be fully examined for patentability. *See* MPEP §809.

Thus, according to MPEP §§ 809 and 821.04(a), at least claims 51-53, all of which depend directly or indirectly from allowable claim 3 should have been considered

in the Office Action of October 24, 2006. Accordingly, Applicants respectfully assert that claims 51-53 should be rejoined with the presently-pending claims and fully examined for patentability in accordance with 37 CFR §1.104.

Furthermore, in the Restriction Training Material for Examiner's for Art Units 1630/1640/1650, Example 1 provides that polynucleotides, vectors and host cells comprising the polynucleotide are placed into the same group. (*See* TC1600 Restriction Training Materials, 2004, page 27.) By withdrawing claims 55-57, 59-61 and 63-65 from consideration, the Examiner is making an improper restriction according to the guidance found in the training materials. Applicants respectfully request that claims 51-53, directed to the vector and host cells comprising the vector, be rejoined and fully examined for patentability.

(ii) Claims 55-57, 59-61 and 63-65

Claims 55-57, 59-61 and 63-65 should be rejoined and fully examined for patentability in accordance with 37 CFR §1.104 because they depend directly or indirectly from claims 47-49, which are believed to be in condition for allowance. Although the Examiner has rejected independent claims 47-49 under 35 U.S.C. §112, first paragraph, this rejection is believed to have been overcome, by the present amendments and remarks. *See* MPEP §821.04(a). Claims 55-57, 59-61 and 63-65 are directed to compositions such as recombinant vectors and genetically engineered host cells, requiring either the allowable product of claim 3 (SEQ ID NO: 115), or sequences that have 95% or 99% identity with SEQ ID NO: 115. In the Office Action of October 24, 2006, the Examiner effectively restricted claims 55-57, 59-61 and 63-65 from the

present application by withdrawing them as being allegedly directed to a non-elected invention. (OA at page 2.) Applicants respectfully traverse this restriction.

Section 821.04(a) of the MPEP states that when restriction has been required between independent or distinct products, or between independent or distinct processes, and all claims directed to an elected invention are allowable, any restriction requirement between the elected invention and any nonelected invention that depends from or otherwise requires all the limitations of an allowable claim should be withdrawn. *See* MPEP §821.04(a). In this case, although genetically engineered host cells and recombinant vectors could technically be classified into a different class and subclass than the polynucleotide, the search for SEQ ID NO:115 or sequences having 95% or 99% identity with SEQ ID NO: 115 would be coextensive with the search of the different classes comprising host cells and recombinant vectors that comprise the polynucleotide.

As discussed above, the Examiner stated in the Office Action of October 24, 2006, that SEQ ID NO: 115 is found to be free of the prior art. (OA, page 4). Thus, any composition that includes SEQ ID NO: 115 and is not a product of nature will also be free of the prior art. Furthermore, Applicants assert that Examination of claims 55-57, 59-61 and 63-65 would not impose a burden on the Examiner because the Examiner has not established that the search for SEQ ID NO:115 would not have provided results pertinent to these claims. *See* MPEP §808.02. Accordingly, since claims 55-57, 59-61 and 63-65 are directed to compositions encompassing an allowable product, Applicants respectfully request that they be rejoined and fully examined for patentability in accordance with 37 CFR §1.104.

Rejections under 35 U.S.C. § 112, first paragraph

A. Claims 47 and 48 do not contain new matter

The Examiner has rejected claims 47 and 48 under 35 U.S.C. § 112, first paragraph, asserting that the amendments of September 13, 2006, and January 24, 2007, introduce new matter that was not described in the specification in such a way as to reasonably convey to one skilled in the art to that the inventor had possession of the inventions as now claimed. (OA at page 3.) Applicants respectfully traverse this rejection.

The specification and claims, as originally filed, provide proper descriptive support for the amendments of September 13, 2006, and January 24, 2007, including the subject matter of claims 47 and 48. Presently-pending claims 47 and 48 are directed to an isolated polynucleotide comprising a nucleic acid sequence from 95-100% identical to the sequence of SEQ ID NO: 115, wherein the isolated polynucleotide encodes a toxin capable of binding to a sodium channel.

Written description does not require that the subject matter of the claim need be described literally, *i.e.*, using the same terms or *in haec verba*, in order for the disclosure to satisfy the description requirement. If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met. *See,* e.g., *Vas-Cath, Inc. v Mahurkar*, 935 F.2d 1555 at 1563 (Fed. Cir. 1991); *Martin v. Johnson*, 454 F.2d 746, 751(CCPA 1972) (stating "the description need not be in *ipsis verbis* [*i.e.*, "in the same words"] to be sufficient"); *see also* MPEP §2163.

Additionally, the "Methodology for Determining Adequacy of Written Description" found at section 2163.II.A.2. of the MPEP provides that, prior to determining whether the disclosure satisfies the written description requirement for the claimed subject matter, an Examiner should review the claims and the *entire specification, including the specific embodiments, figures, and sequence listings*, to understand how the Applicant provides support for the various features of the claimed invention.

In this case, a skilled artisan would have understood the inventor to be in possession of the claimed invention based on the disclosure in the specification and sequence listing as originally filed, which provide descriptive support for the nucleic acid sequences that are at least 95% and 99% identical to SEQ ID NO:115. For example, Table 1, column D, on page 3 of the specification discloses a list of 71 nucleic acid sequences[1] that encode isolated scorpion toxins. (*See* specification at page 3.) Table 1 and the sequence listing are part of the specification, and should be considered when evaluating the adequacy of the written description.

Species	SEQ ID nucleic acid coding region of mature toxin	% identity with SEQ ID 115	SEQ ID primary protein structure of mature toxin	% identity with SEQ ID 116
C. exilicauda	43	86.5 %	44	75%
C. exilicauda	47	87 %	48	76.5%
C. nocius	91	87.7%	92	74.2%
C. elegans	111	82.8%	112	73.3%
C. elegans	**115**	**100%**	**116**	**100%**
C. elegans	119	99.5%	120	95.3%
C. sculpturatus	151	88.5%	152	79.6%
C. sculpturatus	195	88%	196	76.5%

[1] These sequences also appear in the sequence listing as originally filed.

The sequences in the above table are those sequences that share the closest homology with SEQ ID NO:115 as determined by Examiner Desai's sequence search. (*See* APPENDIX A, provided in the response filed January 24, 2007). The percent homology that each molecule listed in Table 1 has with SEQ ID NO:115 is an inherent feature of each sequence described in the specification. The percent homology between the sequences is a fact based on the structure of the sequences disclosed in the specification and sequence listing. The determination of percent identity between nucleic acid sequences was within the skill of the ordinary artisan as of the filing date of this application.

The sequences listed in the above table are part of the specification as-filed. As shown in the above table, SEQ ID NOs: 43, 47, 91, 111, 119, 151, and 195 share 86.5%, 87%, 87.7%, 82.8%, 99.5%, 88.5%, and 88% sequence identity with SEQ ID NO:115, respectively. Applicants assert that the specification as-filed, including the sequence listing, would have reasonably conveyed to one skilled in the relevant art that the inventors had possession of the claimed nucleic acid sequences having 95% or 99% identity with SEQ ID NO:115 at the time the application was filed. Therefore, the specification provides adequate written description under 35 U.S.C. §112, first paragraph, for a range of sequences which possess from 95% to 100% sequence similarity with SEQ ID NO:115, as recited in claims 47-49. Accordingly, this rejection is believed to have been overcome. Reconsideration and withdrawal of the New Matter rejection of claims 47-49 is respectfully requested.

B. The specification provides proper written descriptive support for claims 47 and 48

The Examiner has rejected claims 47 and 48 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. More specifically, the Examiner asserts that the recited subject matter was not described in "the specification in such a way as to convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." (OA at pages 3-4.) The Examiner also asserts that "[o]ne of skill in the art cannot visualize or recognize which nucleic acid sequences can be modified and/or mutated such that the polynucleotide with reduced percent identity retains the function of a toxin affecting sodium and potassium channel activity as disclosed for SEQ ID NO:115." (OA at pages 3-4.) Applicants respectfully traverse this rejection.

The specification as-filed provides adequate written descriptive support for the nucleic acids recited in claims 47 and 48, because a person of ordinary skill at the time of filing could have visualized or recognized the identity of the members of the recited genus based on recited functional requirements and known structural similarities shared by polynucleotides that are at least 95% and 99% identical to SEQ ID NO:115. More specifically, the ordinary artisan reading the specification in conjunction with what was generally known in the art of scorpion toxins would have known that the sequences that are at least 95% or 99% identical to SEQ ID NO:115 would need to bind to the Na^+ channel and possess four cysteine bonds to fall within the scope of claims 47 and 48.

An objective standard for determining compliance with the written description requirement of 35 U.S.C. §112, first paragraph, is, "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed?"

In re Gosteli, 872 F.2d 1008, 1012 (Fed. Cir. 1989), *see also* MPEP 2163.02. An applicant may show possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. *See Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572 (Fed. Cir. 1997). Moreover, the disclosure of a species has also been found to be sufficient to support a claimed genus when the disclosure of species would lead a person of ordinary skill to the genus. *See In re Herschler*, 591 F.2d 693 (CCPA 1979); *see also* MPEP 2163.05). In *Herschler,* the Court held that the disclosure of one corticosteroid was sufficient to support "physiologically active steroid" because the use would lead one of ordinary skill to the entire class of compounds. 591 F.2d at 697. The Federal Circuit has held that when generic elements of a claim are so well known and thoroughly characterized in the art that their recitation alone is sufficient to convey distinguishing information regarding their identity, the written description requirement for those elements is fully satisfied. *See Amgen Inc. v. Hoechst Marion Roussel Inc.*, 65 U.S.P.Q.2d 1385, 1398 (Fed. Cir. 2003). Another important consideration in assessing written description of a claimed invention is the knowledge of one skilled in the art. *See Bilstad v. Wakalopulos*, 386 F.3d 1116, 1126 (Fed. Cir. 2004).

(i) The encoded toxins of claims 47 and 48 must be capable of binding to Na+ channels

In this case, claims 47 and 48 have been amended to recite an isolated polynucleotide comprising a nucleic acid sequence from 95-100% identical to the sequence of SEQ ID NO: 115, wherein the isolated polynucleotide encodes a toxin capable of binding to a sodium channel. As discussed above, the specification as-filed,

including the sequence listing, provides proper written descriptive support under 35 U.S.C. §112, first paragraph, for polynucleotides that are at least 95% and 99% identical to SEQ ID NO:115, as recited in claims 47 and 48. Furthermore, all of the publications cited in the specification have been incorporated by reference in their entirety, and thereby provide additional descriptive support for the presently pending claims. (*See*, e.g., specification paragraph [0105]).

Applicants explain in the specification that scorpion toxins generally fall into two categories: the long chain toxins, 60-76 amino acids in length, which block the Na^+ channel in excitable cells; and the short chain toxins, 29-41 amino acids in length that affect K^+ channels. (specification paragraph [0004]). The claimed toxins are all Na^+ channel toxins, 60-76 amino acids in length, and they all bind to the membrane-bound sodium channel. (specification paragraph [0005]). It is the binding of the toxin to the cation channel (the Na^+ channel) that causes most of the toxicological symptoms in a patient. (specification paragraph [0009]; *see also*, Dehesa-Davilla, page 225).

The specification describes isolated and purified scorpion toxin nucleic acid sequences in the sequence listing, as well as in Table 1. The ordinary artisan reading the specification in light of what was known in the art would have recognized that the claimed sequences fall into the genus of long chain Na^+ channel blocking toxins. (*See* specification paragraph [0004]). Thus, the ordinary artisan as of the filing date would have understood that claims drawn to SEQ ID NO:115 or sequences having 95% and 99% sequence identity with SEQ ID NO: 115 are directed to Na^+ channel blocking toxins.

(ii) The encoded toxins of claims 47 and 48 posses a common structural motif

The Na^+ channel toxins from scorpions also possess a common structural motif. Applicants explain in the specification that these Na^+ channel affecting scorpion toxins posses eight cysteine residues that form four cysteine bonds in the mature toxin. (specification paragraph [0004]; *see also Possani et al.* at page 290, column 2). The common structural motif consists of one stretch of α-helix, plus three strands of β-sheet in antiparallel arrangement, connected by variable regions forming loops. (specification paragraph [0004]; *see also* Possani *et al.* p 287, 290). The cysteine residues are numbered consecutively 1-8 from the N- to the C- terminal of the toxin. Cysteine residues 1 and 8, 2 and 5, 3 and 6, as well as residues 4 and 7 form the four disulfide bridges. These disulfide bonds are conserved in all of the Na^+ channel blocking scorpion toxins that were known as of the filing date of the presently-pending application, including the sequences disclosed in the specification. (specification paragraph [0004]; *see also* Possani *et al.* p 290, column 2; *see also* APPENDIX B previously provided in the response of January 24, 2007, which shows a sequence alignment of the sodium channel toxins disclosed in the specification, and highlights the conserved cysteine residues). In fact, as of the filing date of the present application, all Na^+ channel-specific toxins were known to be stabilized by four disulfide bridges. (specification paragraph [0004]; *see also* Possani *et al.* p 287). Thus, the ordinary artisan reading the specification in light of what was known in the art would have recognized and understood that the recited sequences having 95% and 99% sequence identity with SEQ ID NO: 115 would also possess the conserved structural motif of four cysteine bonds.

Based on the combination of what was known in the art about scorpion toxins at the time of filing and the disclosure of two species of nucleic acid that fall within the scope of claims 47 and 48, the specification conveys to one of ordinary skill in the art that the recited polynucleotides fall into the genus of long chain Na^+ channel-blocking toxins possessing a conserved structural motif of four cysteine bonds.

(iii) The specification as filed provides proper written descriptive support for claims 47 and 48

In the AA, the Examiner asserted that "[i]dentification of one species of a scorpion toxin that has 82.8% identity to SEQ ID NO: 115 (SEQ ID NO: 111) does not describe a genus of polynucleotides, which are at least 83% identical to SEQ ID NO: 115 that encodes toxins that bind sodium channels." Applicants' respectfully traverse this rejection.

Claims 47 and 48 have been amended to recite an isolated polynucleotide at least 95-99% identical to SEQ ID NO: 115. These amendments have been made solely in an effort to advance prosecution, and not in acquiescence of the Examiner's rejection.

Claims 47 and 48 as amended find proper written descriptive support in the specification as filed. Here Applicants have identified one additional species that falls within the genus of polynucleotides with at least 95% sequence identity to SEQ ID NO: 115, and encodes a toxin capable of binding a sodium channel. Claim 47 and 48 are directed to polynucleotides. Polynucleotides encode proteins, and in the presently-amended claims the encoded protein must be capable of binding to a Na^+ channel. Thus, Applicants are claiming a structure that possesses a particular function. The specification has identified one additional species that is encompassed by the genus

having at least 95% sequence identify to SEQ ID NO:115, and possessing the activity recited in claims 47 and 48. More specifically, SEQ ID NO: 119 is a species that falls within the genus of sequences with at least at least 95 % sequence homology to SEQ ID NO: 115, and which encode a toxin capable of binding to a sodium channel. Thus, the specification provides adequate written description under 35 U.S.C. §112, first paragraph, for an isolated polynucleotide as recited in presently-amended independent claims 47 and 48, as well as those claims which depend therefrom.

(iv) The USPTO's Written Description Guidelines support a finding of proper written descriptive support for claims 47 and 48

The USPTO's "*Revised Interim Written Description Guidelines Training Materials*" (hereinafter, "*Guidelines*") provides 18 examples describing how to determine whether the written description requirement of 35 U.S.C. §112, paragraph 1, is satisfied. The facts set forth in Example 14 are almost identical to the present situation, and support a finding of proper written descriptive support for presently-amended claims 47 and 48.

First, the language of claims 47 and 48 is extremely similar in form and substance to that of the sample claim provided in Example 14, which recites:

> A protein having SEQ ID NO: 3 and variants thereof that are at least 95% identical to SEQ ID NO: 3 and catalyze the reaction of A→ B.

Guidelines, p. 53. Similarly, presently-amended claims 47 and 48 require that the claimed polynucleotide is at least 95% identical to SEQ ID NO:115 (the reference compound) and encodes a toxin that is capable of binding to a sodium channel, which is

an essential feature of the claimed invention. Thus, the first requirement of Example 14 is met.

Second, the *Guidelines* state that a search of the prior art indicated that exemplified SEQ ID NO: 3 was novel and unobvious. *Id.* at page 54. In the present case, the Examiner stated in the Office Action of October 24, 2006, that the prior art does not describe an isolated nucleic acid comprising SEQ ID NO: 115, which is recited in claims 47 and 48 (OA at page 4.) Thus, the second requirement set forth in Example 14 has been satisfied with regard to currently pending claims 47 and 48.

Third, the *Guidelines* state an actual reduction to practice of a single disclosed species was deemed sufficient to support the recited genus of proteins that must be variants of exemplified SEQ ID NO: 3. *See Guidelines*, p. 54. The *Guidelines* state that the actual reduction to practice of one species was sufficient because all of the variants were required to possess the specific functional activity and had a high percent structural identity with the reference compound. *See Guidelines*, p. 54. In the present case, Applicants have shown possession of the claimed invention by a reduction to practice as evidenced by the descriptive support for at least seven sequences that fall within the scope of the claims, as well as support for the functional element of the claims. (*See* specification, Table 1, and the sequence listing). Thus, the third requirement set forth in Example 14 of the *Guidelines* has been satisfied.

Fourth, Example 14 of the Guidelines requires that procedures for making variants of exemplified SEQ ID NO:3 which have 95% identity to SEQ ID NO:3 and retain its activity were conventional in the art at the time of filing. *See Guidelines*, p. 53. In the present case, methods for making variants that are at least 95% identical to the

reference compound were known in the art at the time of filing, and are described in our specification. (*See Molecular Cloning: A Laboratory Manual* (2nd ed.), Sambrook *et al.* (Cold Spring Harbor Lab. Press, 1989), chapters 15-18; *see also* specification [0040]). Thus, the fourth requirement set forth in Example 14 of the *Guidelines* has been satisfied with regard to presently pending claims 47 and 48.

Fifth, in Example 14, an assay was described in the specification that identified the other proteins having the binding activity recited in the example claim. *See Guidelines*, p. 53. In the present case, the toxins that are at least 95% or 99% identical to SEQ ID NO:115 can easily be tested for their binding to the Na^+ channel. (*See* specification paragraph [0005]; *see also* Couraud *et al.* p. 10-12.) Although there are many different ways to test the binding of a toxin to a Na^+ channel, one test described in the specification through an incorporated reference uses a rat synaptosome and a labeled toxin. (*See* specification paragraph [0005]; *see also* Couraud *et al.* p. 10-12). Thus, the fifth requirement set forth in Example 14 of the *Guidelines* has been satisfied with regard to presently pending claims 47 and 48.

Based on the requirements set forth in Example 14 of the USPTO's *Revised Interim Written Description Guidelines Training Materials*, the exemplified claims recite a common structural motif that has a specific functional requirement. The present specification conveys to a person of ordinary skill in the art that the inventors had possession of, and broadly described, an isolated polynucleotide comprising a nucleic acid sequence from 95-100% identical to SEQ ID NO:115, wherein the isolated polynucleotide encodes a toxin that is capable of binding to a sodium channel, as recited in claims 47 and 48. Thus, the specification provides adequate written description under

35 U.S.C. §112, first paragraph, for an isolated polynucleotide as recited in presently-amended independent claims 47 and 48, as well as those claims which depend therefrom. Accordingly, this rejection is believed to have been overcome. Reconsideration and withdrawal of the rejection of claims 47 and 48 is respectfully requested.

(v) The USPTO's Written Description Guidelines support a finding of proper written descriptive support for claims 47-49

In the AA of February 21, 2007, the Examiner rejected Applicants comparison of the claimed invention with Example 14 of the *Guidelines*. The Examiner alleged that "Example 14 in the Training Materials is drawn to a protein with a known function, whereas the current pending claims are drawn to a polynucleotide. It appears Example 11 is more representative of the present situation." (AA page 2.) Applicants respectfully traverse this rejection.

The present claims are directed to polynucleotides, specifically, polynucleotides having a particular sequence similarity to SEQ ID NO: 115, and these polynucleotides must encode proteins capable of binding Na^+ channels. The claims are not directed at isolated alleles, as described in Example 11. The polynucleotides of the present claims encode a toxin (a protein) that is capable of binding to a Na^+ channel. Thus, it is clear that the polynucleotides are not directed at genomic polynucleotide sequences, but instead are coding polynucleotides, or cDNA's. Because none of the claims are directed to isolated alleles, the comparison to Example 11 of the *Guidelines* is inapt. Applicants respectfully request that this rejection be reconsidered and that it be withdrawn.

(vi) The USPTO's Written Description Guidelines support a finding of proper written descriptive support for claims 71 and 76

Applicants have added new claims 71-80, directed to polynucleotides encoding a protein sequence and vectors encoding the polynucleotides. The language of new claims 71 and 76 are nearly identical in form and substance to that of the sample claim provided in Example 11, which recites:

1. An isolated DNA that encodes protein X (SEQ ID NO:2).

Guidelines, p. 41. Similarly, claims 71 and 76 require that the claimed polynucleotide encode SEQ ID NO: 44, SEQ ID NO: 48, SEQ ID NO: 92, SEQ ID NO: 112, SEQ ID NO: 116, SEQ ID NO: 120, SEQ ID NO: 151 and SEQ ID NO: 195. According to the *Guidelines*, the recitation of a single polynucleotide species that falls within the genus of polynucleotides is sufficient to establish proper written descriptive support. *Guidelines*, p. 41. A person of skill in the art "could readily envision all the DNAs degenerate to SEQ ID NO:1 by using a genetic code table." *Guidelines*, p. 41. The Example concludes that the hypothetical invention encompassed a genus based on genetic coding tables.

In this case, Applicants have disclosed individual polynucleotides set out in the sequences of SEQ ID NO: 43, SEQ ID NO: 47, SEQ ID NO: 91, SEQ ID NO: 111, SEQ ID NO: 115, SEQ ID NO: 119, SEQ ID NO: 150 and SEQ ID NO: 194. These polynucleotide sequences encode the polypeptide sequences set out in SEQ ID NO: 44, SEQ ID NO: 48, SEQ ID NO: 92, SEQ ID NO: 112, SEQ ID NO: 116, SEQ ID NO: 120, SEQ ID NO: 151 and SEQ ID NO: 195. Following Example 11 of the *Guidelines*, Applicants' disclosure of a polynucleotide that encodes a polypeptide provides support for the genus of polynucleotides based on the genetic coding table. Thus, the

specification provides adequate written description under 35 U.S.C. §112, first paragraph, for an isolated polynucleotide, as recited in presently-amended independent claims 71 and 76, as well as those claims which depend there from.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

Laura Vogel

Laura A. Vogel
Attorney for Applicants
Registration No. 55,702

Date: June 25, 2007

1100 New York Avenue, N.W.
Washington, D.C. 20005-3934
(202) 371-2600
679038_1.DOC